UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/611,527	06/30/2000	Lewis T. Williams	PP-01598.002 / 200130.512	5701

27476 7590 02/26/2003

Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/611,527	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *December 06, 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *2-8,11,12,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 9, 10, and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-15* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traversal of Group I, claims 1-10 and 13, Species C (a generic library), and SEQ ID NO:591, in Paper No.10, filed December 06, 2002, is acknowledged.

2. The traversal is on the ground(s) that it would not be unduly burdensome to perform a search on claims 1-15 together. This is not found persuasive because nucleic acids and polypeptides are directed to different chemical types regarding the critical limitations therein. Further, the distinct methods of use corresponding to each chemical type support the undue search burden if they were examined together. While taking advantage of the distinct properties of each chemical type, these usages have distinct goals as requiring distinct and different functions and results thereof without overlapping search due to different subject matter. This lack of overlapping searches documents the undue search burden if they were search together.

3. Further, Applicants argue that it would not be an undue burden to examine more than one sequence. The traversal to limiting the number of nucleic acid sequences to one was found unpersuasive because, due to the number of these requests made, it is practically impossible to accommodate all requests. The overwhelming number of sequences poses undue search burden when more than one nucleic acid sequence is elected, thus making the previous waiver to a complete search of all of the sequences of this instant application, effectively impossible to reasonably implement.

4. The requirement is still deemed proper and is therefore made FINAL.

5. Claims 2 and 3 are withdrawn from examination because they are directed to libraries that are not of the elected species C (a generic library).

6. Claims 4-8 are withdrawn from examination because they are directed to SEQ ID NOs that are not of the elected SEQ ID NO:591.

7. Claims 1, 9, 10 and 13 which are directed to Species C (a generic library) and SEQ ID NO:591 are examined on the merits.

Objections

8. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (Page 54, Lines 5-6). Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code, or inactivate the hyperlink. See MPEP § 608.01.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). See, for example, Page 54, lines 12, 20-22, and 31-32, and on page 55, lines 9-10 and thereof. However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because these sequences contain polypeptide sequences with sequence lengths that are equal to or greater than 4 polypeptide molecules and these sequences do not have SEQ ID Nos cited along with each sequence in the specification. Applicants are also reminded that SEQ ID Nos are not required in Figures per se, however, the corresponding SEQ ID Nos then are required in the Brief Description of the Drawings section in the specification. Applicants are also reminded that a CD-ROM sequence listing submission may replace the paper and computer readable form sequence listing copies. Applicant(s) are required to submit a new computer readable form sequence listing, a paper copy for the specification, statements under 37 CFR § 1.821(f) and (g),

if there is a need to list additional sequences in the listing. Applicant(s) are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 9, 10 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Specific to claim 9, lines 1-3, the phrase "a degenerate variant" cause the claim to be vague and indefinite. It is unclear what criteria is being used to determine that a particular nucleotide sequence is a degenerate variant of SEQ ID NO:591. Is a nucleotide sequence considered to be a degenerate variant because it is different in sequence length, the encoded protein has a different molecular weight or the nucleotide sequence or the encode protein has a different cellular distribution? Or a nucleotide sequence is considered a degenerate variant because an encoded amino acid of SEQ ID NO:591 could be encoded by more than one codon? Clarification of the metes and bounds is required. Claims 10 and 13 are rejected due to being dependent from claim 9.

LACK OF UTILITY UNDER 35 U.S.C. § 101:

12. The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph,

"Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

13. The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

14. Claims 1, 9, 10 and 13 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

15. The critical limitation of claims 1, 9, 10 and 13 is a library of the claimed polynucleotide SEQ ID NO: 591. While some expression data are supplied for several sequences in Tables 7-22, pages 76-98, no data therein indicate any specificity regarding the elected SEQ ID NO:591. The claimed nucleic acid is not supported by a specific asserted utility because the other

disclosed uses (not specified for any particular sequence) mentioned in the specification are generally applicable to many nucleic acids. The specification states that the polynucleotide sequences may be useful in the detection of expression levels, mapping, tissue profiling, forensics, genetic analysis and diagnostic applications (Pages 25-27). The above-mentioned list of desirable utility for the claimed sequence falls short of a readily available utility. These are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the polynucleotide being claimed.

16. Further, the claimed polynucleotide is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case, the protein produced as a final product resulting from processes involving the nucleic acid does not have asserted or identified specific and substantial utilities. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved, such as the protein encoded by SEQ ID NO: 591, does not define a "real world" context for use. Similarly, the other listed utilities and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to many such compounds.

17. Furthermore, Applicants do not disclose whether normal or tumor tissue was the source of SEQ ID NO:591. Thus, there is no disclosure of a possible utility for SEQ ID NO:591, for example, for testing for a tumor via differential expression versus normal tissue. It is

acknowledged that Applicants disclose in Examples 6-12, pages 80-99, polynucleotides differentially expressed in high metastatic potential cancer cells versus low metastatic cancer cells. However, the disclosure in Examples 6-12 does not specifically indicated that SEQ ID NO:591 is differentially expressed in these cells. Or SEQ ID NO:591 is specifically expressed in normal versus cancer tissues or cells. Therefore, Applicants fail to provide sufficient disclosure for SEQ ID NO:591 in regard its tissue source or expression in normal versus cancer tissue further supports that SEQ ID NO:591 lacks specific and substantial utility.

18. It is acknowledged that Applicants disclose in Examples 1-3 that SEQ ID NO:591 was derived from cell lines and human normal and tumor tissue cDNA libraries (Page 50, lines 5 and 7). The sequence was used in a BLASTN vs. GenBank search. After subsequent filtering steps, novel sequences resulted from the sequence search were assigned SEQ ID NOS:1-3351 (Example 1, Page 51). SEQ ID NOS:1-3351 were translated in all three reading frames to determine the best alignment with the individual sequences by searching public databases to identity the function of gene products (Example 2, page 52). Applicants also disclose that profile searches were performed with SEQ ID NOS:1-3351 to identify members of protein families (Example 3, Page 53). However, the disclosure of the similarity of a particular sequence to another by sequence comparison without specific and substantial disclosure as to the specific identity and function of a nucleotide composition as defined by specific and substantial biological activity does not support the claimed asserted utility of the said composition. It is noted that applicant has identified a sequence which is known in the prior art and which has a stated sequence similarity to the claimed sequence. Absent factual biological activity data, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably

support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence. Furthermore, it is unclear whether the similar sequence identified in the prior art has actually been tested for the biological activity or whether this also is an asserted biological activity based upon sequence similarity to yet a different sequence.

19. Note that it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual biological activity data characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Lopez et al. (Molecular Biology, 32:881-891,1999); Attwood (Science, 290:471-473, 2000); Gerhold et al. (BioEssays, 18(12):973-981, 1996); Wells et al. (Journal of Leukocyte Biology, 61(5):545-550, 1997); and Russell et al. (Journal of Molecular Biology, 244:332-350, 1994). However, this level of factual biological activity data is absent here.

20. It is noted that nucleic acids and corresponding vectors and host cells may have a generally credible utility of some type, but that the criteria for utility being specific and substantial must also be met, if there is no well established utility for the claimed invention.

There is no known well-established utility for the instantly claimed invention, which is under examination.

Claims Rejected Under U.S.C. § 112, First Paragraph

21. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF ENABLEMENT

22. Claims 1, 9, 10 and 13 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed sequence.

23. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

24. Due to the undue quantity of experimentation necessary to determine activity or property of the disclosed nucleic acid such that it can be determined how to use the claimed library comprising the said nucleic acid, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, and the breadth of the claims which fail to recite particular biological activities, the specification fails to teach the skilled artisan how to make and use the claimed library comprising SEQ ID NO:591.

25. Also, since the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above (refer to 35 U.S.C. § 101 rejection), one skilled in the art would not know how to use the claimed invention.

LACK OF WRITTEN DESCRIPTION

26. Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

27. The specification discloses SEQ ID NO: 591, which corresponds to DNA encoding a protein. Claim 9 is directed to encompass gene sequences, sequences having at least 90% sequence identity to SEQ ID NO:591 and degenerate variants or fragment thereof. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

> Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does

> not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

28. With the exception of SEQ ID NO: 591, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

> University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that: ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

29. Therefore, only SEQ ID NO: 591 but not the full breadth of the claim 9 meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115)

Claim Rejections - 35 USC § 102

30. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

31. Claim 9 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Product Number O 4128 (Sigma Catalog 1990).

32. Sigma Catalog discloses Product Number O 4128 which is 100% identity to polynucleotide fragment position 22-23 of SEQ ID NO:591 of this instant application.

CONCLUSION

33. NO CLAIM IS ALLOWED.

34. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

35. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

36. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

37. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
2/24/03

ARDIN H. MARSCHEL
PRIMARY EXAMINER